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Optimal Use of Directional Coronary Atherectomy Is Required to Ensure Long-Term Angiographic Benefit: A Study With Matched Procedural Outcome After Atherectomy and Angioplasty

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Objectives. This study was designed to examine whether restenosis is related to the extent or mechanism of lumen improvement and to explore angiographic determinants of optimal atherectomy.

Background. Directional atherectomy induces a greater extent of immediate gain and late loss but has not been found to yield a better late angiographic lumen than angioplasty in randomized trials. The difference in lumen renarrowing may be related to either the extent or the mechanism of immediate gain. The design of previous studies has precluded the detection of a device-specific effect on restenosis.

Methods. A retrospective analysis was based on matching a prospectively collected series of 80 native coronary arteries successfully treated with atherectomy with a prospectively collected series of 80 native coronary arteries successfully treated with balloon angioplasty. Angiographic analysis was performed in 160 lesions to explore whether a specific device-related effect exists. Multivariate analyses were performed to determine the correlates of minimal lumen diameter at follow-up and late lumen loss and to identify the procedural characteristics for optimal atherectomy.

Results. Matching resulted in two comparable groups with equivalent baseline clinical and stenosis characteristics. By study design, atherectomy and angioplasty resulted in similar mean (±SD) immediate lumen gain (1.15 ± 0.44 vs. 1.10 ± 0.40 mm, p = 0.50). However, lumen loss was more pronounced after atherectomy, and, thus, the minimal lumen diameter at follow-up differed significantly between the two groups (1.78 ± 0.57 vs. 2.00 ± 0.56 mm, p = 0.001). Device type was retained in the multivariate analysis as an independent predictor of late minimal lumen diameter and lumen loss. Multivariate analysis identified vessel size and immediate gain as determinants of optimal atherectomy.

Conclusions. Restenosis is a consequence not only of the extent of lumen improvement but also of the mechanism of vessel wall injury (debulking vs. dilating). While performing atherectomy, the operator should strive for an optimal procedural result to accommodate an increased intimal hyperplastic response.

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It has been conclusively demonstrated (1–11) that a large postprocedural diameter achieved at coronary intervention yields a greater long-term residual lumen diameter. However, it has not been shown whether this angiographic outcome is also related to the specific mechanism of the interventional device deployed. Thus far, the design of coronary interventional studies has precluded the detection of a device-specific effect on lumen renarrowing. In particular, previous studies have been confounded by the effects of unequal vessel size and immediate lumen gain (3,4,7), which have been shown to be independent predictors of restenosis (4,5,9).

When we first studied the differences between restenosis after atherectomy and balloon angioplasty in a matched series (7), we observed a significant difference in lumen renarrowing between the two devices when deployed in vessels of similar size. Specifically, late loss was larger in the atherectomy than angioplasty group (0.68 vs. 0.23 mm). Although we believed that this effect was due to the superior immediate lumen gain with consequent greater lumen loss associated with atherectomy, we recognized that the difference in lumen renarrowing after atherectomy and angioplasty may relate to either the extent *or* the mechanism (debulking vs. dilating) of lumen improvement ("vessel wall injury"). Therefore, the purpose of this study was to extend our observations and to test the hypothesis that each device has unique properties with respect to lumen renarrowing that are independent of vessel size and lesion severity and lumen gain. Therefore, we compared the long-term angiographic outcome of directional coronary atherectomy and conventional balloon angioplasty in a prospectively collected series of 160 patients with comparable vessel size, lesion severity and lumen gain. Multivariate analyses were performed to determine the correlates of minimal lumen diameter at follow-up and late lumen loss and to identify the angiographic characteristics of optimal atherectomy. The immediate and late changes in stenosis geometry were assessed by quantitative coronary angiography.

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Table 1. Clinical and Angiographic Characteristics of the Study Patients

	Atherectomy		Angioplasty, Matched Group (n = 80)	p Value*
	Nonmatched Group (n = 26)	Matched Group (n = 80)		
Age (yr)	58 ± 12	57 ± 11	58 ± 10	NS
Male (%)	70	81	91	NS
Vessel treated (%)				
LAD	59	65	25	
LCx	7	12	19	0.001
RCA	33	22	56	
Unstable angina (%)	38	30	37	NS
Previous infarction (%)	31	27	36	NS
Previous CABG (%)	0	1	2	NS
Diabetes (%)	4	2	6	NS
Hypercholesterolemia (%)	24	15	20	NS
Multivessel disease (%)	23	25	32	NS
Reference diameter (mm)	3.64 ± 0.93	3.21 ± 0.49	3.22 ± 0.48	NS
MLD (mm)	1.34 ± 0.52	1.16 ± 0.32	1.16 ± 0.28	NS
Diameter stenosis (%)	63 ± 12	64 ± 10	63 ± 9	NS
Area stenosis (%)	83 ± 17	84 ± 16	84 ± 17	NS

*Matched atherectomy-treated versus matched angioplasty-treated group. Data presented are mean value ± 1 SD, unless otherwise indicated. CABG = coronary artery bypass graft surgery; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; MLD = minimal lumen diameter; RCA = right coronary artery.

Methods

Patients. *Atherectomy group.* Between September 1989 and March 1993, 178 patients underwent 184 directional atherectomy procedures for native coronary or bypass graft lesions. Of these, 120 consecutive patients (who underwent 127 successful *stand-alone* procedures) had follow-up angiography at 6 months. For the purpose of this study, the late outcome of atherectomy was compared with that of angioplasty for consecutive native primary lesions. Therefore, patients with restenotic lesions, lesions with postatherectomy adjunctive balloon angioplasty and patients with a subacute coronary occlusion <24 h were excluded. Of the 120 patients, 3 were treated for a lesion in a venous bypass graft, and 13 had atherectomy for 18 restenotic lesions after a previous angioplasty. Therefore, 104 patients who underwent 106 successful atherectomy procedures for native primary coronary artery disease were eligible for matching. Ultimately, 80 patients with 80 coronary artery lesions were individually matched with patients undergoing successful balloon angioplasty; the remaining 26 patients could not be matched. The clinical and angiographic details of the atherectomy and angioplasty groups are presented in Table 1.

Before atherectomy, patients had documented myocardial ischemia that required revascularization. Patients were selected for directional atherectomy when they presented with a stenosis in a proximal nontortuous coronary artery with a presumed reference diameter >2.5 mm. All patients gave informed consent and were prospectively scheduled for follow-up angiography at 6 months, which was completed in 92%. The study was approved by the hospital's Institutional Review Board. All clinical and angiographic data were collected prospectively.

Balloon angioplasty group. Patients were collected from the angioplasty data base, which contains clinical and angiographic details of 3,072 patients (mean [±SD] age 56 ± 9 years; 81% men) who underwent 3,736 angioplasty procedures and participated in previous angioplasty restenosis prevention trials in Europe and North America (8,12,13). The majority of the patients (52%) were treated for Canadian Cardiovascular Society class III or IV angina. In the entire angioplasty population, 47% of the dilated lesions were located in the left anterior descending coronary artery, 23% in the left circumflex coronary artery and 30% in the right coronary artery. On baseline quantitative angiography, preangioplasty mean vessel size and minimal lumen diameter were 2.62 ± 0.53 and 1.09 ± 0.29 mm, respectively. The preangioplasty percent diameter and area stenosis were 58 ± 10% and 84 ± 16%, respectively. Balloon dilation in these 3,736 lesions resulted in a postangioplasty minimal lumen diameter and diameter stenosis of 1.77 ± 0.36 mm and 33 ± 8%, respectively. At follow-up the minimal lumen diameter decreased to 1.53 ± 0.47 mm with a concomitant increase in diameter stenosis to 42 ± 14%. The loss index for these 3,736 lesions was 0.30 ± 1.65. An angiographic and clinical follow-up rate of >90% was obtained. Because neither angiographic nor clinical benefit of the tested compounds could be demonstrated in these restenosis trials, the placebo and active treatment groups could be pooled for the present study.

Atherectomy and angioplasty procedures. The procedures were performed as previously described (7,8,12–16). Briefly, the atherectomy device was directed over a guide wire and positioned across the stenosis. The support balloon was then inflated up to 7.5 psi, the cutter was retracted, and balloon

inflation pressure was increased to maximally 45 psi. The driving motor was activated, and the rotating cutter was slowly advanced to cut and collect the protruding atherosclerotic lesion in the collecting chamber located at the tip of the catheter. After every pass the balloon was deflated and either removed or repositioned. Although an optimal angiographic result was sought for each lesion treated, the procedure was considered angiographically successful when the residual diameter stenosis was <50% after tissue retrieval. This classic definition of success should be viewed in the historical perspective, because nowadays a lumen gain of at least 0.7 mm or a postatherectomy diameter stenosis <20% may be deemed necessary before the procedure is considered successful, as recently observed in retrospective analyses (2) and as defined in upcoming atherectomy trials (Balloon Versus Optimal Atherectomy Trial [BOAT], Optimal Atherectomy Restenosis Study [OARS] and European Cardivolol Restenosis trial [EUROCARE]).

Balloon angioplasty was performed with a steerable, movable guide wire system by means of the femoral route. Standard available catheters were used. Choice of balloon type, size as well as inflation duration and pressure were left to the discretion of the operator. Balloon dilations were repeated until the severity of the obstruction was at least <50% diameter stenosis as judged visually by the operator on coronary angiography. After all interventions, the arterial and venous sheaths were usually left in place for 6 h. Patients were monitored for 24 h, and electrocardiograms and cardiac enzyme levels were obtained twice daily. A calcium antagonist was given every 2 h for 24 h after the procedure, and the patients were maintained on aspirin therapy for 6 months.

Quantitative coronary angiography. Quantitative analysis of the coronary segments was performed with the computer-based Coronary Angiography Analysis System (CAAS), which has previously been validated and described in detail (8,12–17). In particular, accuracy and precision measurements for in vivo phantom measurements are 0.09 and 0.23 (18). In essence, boundaries of a selected coronary artery segment are detected automatically from optically magnified and video-digitized regions of interest (512 × 512 pixels) of a cine frame. The absolute diameter of the stenosis in millimeters is determined using the guiding catheter as a scaling device for calibration. The external diameter of each individual catheter is measured by a precision micrometer with a tolerance of 0.001 mm. Correction for pincushion distortion is performed. Computer estimation of the original dimension of the artery at the site of the obstruction provides an interpolated reference diameter. The percent diameter stenosis is then calculated. To standardize the method of analysis of the interventional and follow-up angiograms, the following measures are routinely applied. First, the X-ray gantry is exactly repositioned to the settings that were documented at the time of the intervention. Second, all study frames to be analyzed were selected at end-diastole to minimize foreshortening and blurring effects of systolic motion. Third, the user-determined beginning and end points of a segment of a major coronary artery were identified according to the definitions of the American Heart Association (19). Finally, Polaroid photographs were taken of the video image with the detected contours superimposed to ensure that the analyses were performed on the same coronary segments. Intracoronary isosorbide dinitrate (1 to 3 mg) was given before and after intervention. Administration of intracoronary nitrates was recommended before angiography at follow-up catheterization.

Matching process. To obtain patients with comparable preprocedural and postprocedural stenoses, lesions were matched according to reference diameter, preinterventional and postinterventional minimal lumen diameter. The analysis is thus independent of vessel size, lesion severity and extent of device-induced lumen gain. The process of matching has been previously described (7,16). Briefly, the principles of matching by quantitative angiography are threefold: 1) the angiographic dimensions of matched lesions are assumed to be "identical"; 2) the observed difference between the two "identical" lesions must be within the range of the reproducibility of the CAAS analysis, 0.1 mm (= 1 SD); and 3) the reference diameter of the lesions to be matched are selected within a range of ±0.3 mm (= 3 SD; 99% confidence limits) (8,12,13).

Statistical analysis. The unit of analysis reported here is the stenotic lesion, not the patient. All values are expressed as mean value ± 1 SD. Comparisons of the severity of reference diameter, minimal lumen diameter, diameter stenosis and area stenosis between the two groups were performed using the paired Student *t* test. Levene's test for variance was used to examine the equality of group variability, and if a significant difference was found, the Welch and Brown-Forsythe tests for equality of means were applied. The Bonferroni correction was applied for multiple comparisons. Linear regression analysis by groups was performed (BMDP statistical package) as a formal test for comparison of correlations and slopes. Selected angiographic variables were evaluated by univariate regression analysis for their correlation with absolute lumen loss and for their correlation with minimal lumen diameter at follow-up. Independent contribution of variables was assessed by multivariate stepwise regression analysis using a commercially available statistical software package (SAS, SAS Institute Inc.). Multiple linear regression analysis was utilized to account for the influence of preprocedural minimal lumen diameter, immediate lumen gain and vessel size in evaluating their contribution to the minimal lumen diameter at follow-up and late lumen loss. Differences between categoric variables were tested with the chi-square and Fisher exact tests as appropriate. Differences were considered statistically significant at $p < 0.05$.

Results

Outcome of the matching process. Although 104 patients (106 atherectomy procedures) were eligible for the matching study, 24 patients (26 lesions) could not be matched with a twin balloon angioplasty-treated patient (Table 1). Therefore, the final analysis was performed for 160 patients treated by either

directional atherectomy or balloon angioplasty. The baseline clinical and angiographic characteristics of the atherectomy-treated patients were compared with those of the matched angioplasty-treated group. The 160 patients were predominantly male with a mean age of 57 ± 11 years. Patients were predominantly treated for stable angina according to the American Heart Association classification. Atherectomy was preferentially performed in the left anterior descending coronary artery (65% vs. 25%), and the right coronary artery was more frequently treated by angioplasty (23% vs. 56%, p < 0.001). The incidence of left circumflex artery lesions was similar in both groups (12% vs. 19%). No differences between the groups were found for risk factors for coronary artery disease or preceding cardiovascular events, such as infarction or bypass surgery. By study design, no significant differences between the atherectomy and angioplasty groups were found in baseline quantitative angiographic variables (mean vessel size 3.21 ± 0.49 vs. 3.23 ± 0.48 mm, preprocedural minimal lumen diameter 1.16 ± 0.32 vs. 1.16 ± 0.28 mm, and percent diameter stenosis 64 ± 10 vs. 63 ± 9%, respectively).

Baseline characteristics of the 26 unmatched atherectomy lesions revealed no difference in clinical profile between matched and unmatched patients. Although the percent diameter stenosis and percent area stenosis in the unmatched group were equal to those in the matched group, atherectomy was performed in larger vessels (reference diameter 3.64 ± 0.93 mm) with a concomitant larger preprocedural minimal lumen diameter (1.34 ± 0.52 mm) than in the matched group. Matching with similar angioplasty lesions was not possible because of either a large immediate lumen gain with concomitant low percent residual diameter stenosis or because of large vessel sizes. The 80 matched angioplasty-treated patients had similar clinical and angiographic characteristics compared with the entire angioplasty cohort with respect to gender, age (56 vs. 58 years) and diabetes (6% vs. 7%). By virtue of matching with atherectomy lesions, the matched angioplasty-treated group had larger vessels (3.23 vs. 2.62 mm) and larger minimal lumen diameters (1.16 vs. 1.09 mm) than the entire angioplasty cohort, although their lesion severity was similar (percent diameter stenosis 63% vs. 58%).

Immediate angiographic outcome in matched patients. By virtue of our matching protocol, the preprocedural and postprocedural minimal lumen diameters in both groups were similar (2.31 ± 0.38 vs. 2.26 ± 0.38 mm, p = 0.98, and 2.31 ± 0.38 vs. 2.26 ± 0.38 mm, p = 0.46, respectively) (Table 2). Therefore, the immediate lumen gain achieved with atherectomy was comparable with that achieved at angioplasty (1.15 ± 0.44 vs. 1.10 ± 0.40 mm). Relative gain, defined as gain divided by vessel size, was similar in both groups. In Figure 1, the graphic display of the immediate results after atherectomy and balloon angioplasty are shown. As displayed, the matching process was adequate, with superimposition of the distribution frequency curves of the minimal lumen diameter before and after atherectomy and angioplasty indicating similar preprocedural and postprocedural stenosis severity irrespective of the deployed device.

Table 2. Comparison of Quantitative Angiographic Data in Matched Patients Who Underwent Atherectomy or Balloon Angioplasty

	Atherectomy (n = 80)	Balloon Angioplasty (n = 80)	p Value
Reference diameter Pre (mm)	3.21 ± 0.49	3.23 ± 0.48	NS
MLD			
Pre (mm)	1.16 ± 0.26	1.16 ± 0.32	NS
Post (mm)	2.31 ± 0.38	2.26 ± 0.38	NS
F-up (mm)	1.78 ± 0.57	2.00 ± 0.56	0.01
Diameter stenosis			
Pre (%)	64 ± 10	63 ± 9	NS
Post (%)	28 ± 11	31 ± 10	0.02
F-up (%)	41 ± 18	38 ± 16	NS
Absolute lumen loss (mm)	0.53 ± 0.58	0.26 ± 0.60	0.005
Relative lumen loss	0.18 ± 0.21	0.08 ± 0.19	0.002
Loss index	0.52 ± 0.81	0.17 ± 0.68	0.004
Lesion length (mm)	6.73 ± 2.51	6.90 ± 2.34	NS
Curvature value	15.5 ± 6.9	12.7 ± 5.8	NS
Symmetry index	0.55 ± 0.25	0.44 ± 0.25	NS
Area plaque (mm^2)	9.33 ± 4.94	9.96 ± 4.45	NS

Data presented are mean value ± 1 SD. F-up = at follow-up; MLD = minimal lumen diameter; Post = after intervention; Pre = before intervention.

Late angiographic outcome in matched patients. Angiographic follow-up was obtained in all patients (Table 2). The restenosis rate according to the >50% diameter stenosis categoric criterion was comparable between the atherectomy-treated and angioplasty-treated groups (28% vs. 22%, chi-square 1.038, p = 0.30). Although a similar immediate gain was achieved irrespective of the device used, the atherectomy-treated patients had a significantly higher late loss during follow-up (0.53 ± 0.58 vs. 0.26 ± 0.60 mm, p < 0.005). Therefore, the residual minimal lumen diameter at follow-up was significantly smaller after atherectomy than after angioplasty (1.78 ± 0.57 vs. 2.00 ± 0.56 mm, p < 0.001) (Fig. 1). Relative loss (loss divided by vessel size) and loss index (late loss divided by immediate gain) were significantly higher after atherectomy, indicating a more intense renarrowing process. A linear relation was found between relative gain (injury) and relative loss (repair) in the two groups, with a steeper relative gain/relative loss regression line slope in the atherectomy-treated group (0.56) than in the angioplasty-treated group (0.44), although this difference did not achieve statistical significance because of a wide data scatter (large standard error of the mean).

Multivariate analysis of lumen loss and late residual diameter. To characterize the lumen changes after the intervention according to a continuous approach, two multivariate stepwise models were generated in which 1) residual lumen at follow-up and 2) absolute loss were taken as the dependent variables.

Univariate predictors of *minimal lumen diameter at follow-up* were minimal lumen diameter after intervention, device type and vessel size. In multivariate analysis, vessel size was found to have an independent positive influence on minimal lumen diameter at

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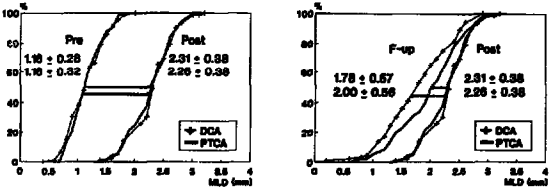

Figure 1. Cumulative frequency curves of the immediate and follow-up (F-up) effects in minimal lumen diameter (MLD) of directional coronary atherectomy (DCA) as assessed by quantitative percutaneous transluminal coronary angiography (PTCA). Pre (Post) = before (after) atherectomy.

follow-up, and device had a comparable negative influence on late residual lumen. Therefore, it is apparent that the late results after successful interventions are superior in larger vessels and that there is a device effect on lumen renarrowing and late minimal lumen diameter at follow-up. The influence of vessel size may in part account for the results observed in new device studies because typically these devices are used in larger vessels. The multivariate model for predicting residual late lumen was found to be the following: Minimal lumen diameter at follow-up = 1.28 + 0.22 Vessel size − 0.23 Device, where angioplasty = 0, and atherectomy = 1.

Minimal lumen diameter after intervention, lumen gain, relative gain, minimal lumen diameter before intervention and device type were univariate predictors for *absolute lumen loss* during follow-up. Of these, lumen gain and device type were retained in the multivariate model to predict the renarrowing process. In multivariate analysis, the relation between gain and loss is demonstrated because immediate gain is found to exert a positive influence on late loss. In addition, preinterventional minimal lumen diameter and device type were positively associated with lumen loss. This may indicate that the use of a bulky device is associated with an increase in late lumen loss because the use of the atherectomy device is associated with an additional late loss of 0.24 mm compared with the use of the balloon. The model for predicting absolute lumen loss in this population can be described by the following equation: Absolute loss = −1.0 + 0.64 Gain + 0.46 Minimal lumen diameter before intervention + 0.24 Device, where angioplasty = 0, and atherectomy = 1.

Optimal atherectomy. In view of the distinct renarrowing properties of the atherotome, we sought to identify which angiographic variables yield independent information for the prediction of late lumen. Therefore, the atherectomy-treated patients were classified according to the median postatherectomy minimal lumen diameter. Table 3 summarizes the changes in stenosis geometry for all atherectomy procedures. A large postprocedural atherectomy lumen was associated with a large vessel (3.48 ± 0.70 vs. 3.13 ± 0.54 mm, p = 0.0001), a large minimal lumen diameter before atherectomy (1.29 ± 0.41 vs. 1.11 ± 0.34 mm, p = 0.02) and a large lumen gain (1.50 ± 0.39 vs. 0.98 ± 0.42 mm, p = 0.0001). Residual diameter stenosis for this group was 20 ± 8%. Although late loss during follow-up was higher (0.86 ± 0.64 vs. 0.42 ± 0.59 mm, p = 0.004), the minimal lumen diameter at follow-up was larger in the group that underwent a favorable compared with the less favorable atherectomy (1.92 ± 0.62 vs. 1.67 ± 0.56 mm, p = 0.03). This preserved favorable long-term angiographic outcome was also reflected in the immediate gain/late loss regression equation, which showed a shallower slope in the optimal than in the suboptimal atherectomy-treated group (0.35 vs. 0.45), although its difference did not reach statistical significance: Loss = 0.33 + 0.35 Gain (r = 0.22, p = 0.1173, optimal group) versus Loss = 0.45 + 0.45 Gain (r = 0.32, p = 0.02, suboptimal group). The restenosis rate, defined as diameter stenosis <50% at follow-up, was lower in the optimal than in the suboptimal group (25% vs. 34%), although it did not reach the level of significance.

Multivariate analysis distinguished vessel size, gain and preprocedural minimal lumen diameter as independent predictors of minimal lumen diameter at follow-up and late loss. Figures 2 and 3 provide a three-dimensional reconstruction of the regression plane for late lumen and late loss. The regression plane is the resultant of loss, gain and minimal lumen diameter before atherectomy. Vessel size may be seen as the fourth

Table 3. Optimal Versus Suboptimal Atherectomy: Lumen Changes After Atherectomy per Minimal Lumen Diameter After Atherectomy

	MLD Post >2.47 mm (n = 53)	MLD Post <2.47 mm (n = 53)	p Value
Reference diameter Pre (mm)	3.48 ± 0.70	3.13 ± 0.54	0.0001
MLD			
Pre (mm)	1.29 ± 0.41	1.11 ± 0.34	0.0208
Post (mm)	2.78 ± 0.27	2.09 ± 0.38	0.0001
F-up (mm)	1.92 ± 0.62	1.67 ± 0.56	0.0317
Diameter stenosis			
Pre (%)	63 ± 10	65 ± 11	NS
Post (%)	20 ± 8	32 ± 10	0.0001
F-up (%)	39 ± 17	44 ± 18	NS
Gain (mm)	1.50 ± 0.39	0.98 ± 0.42	0.0001
Loss (mm)	0.86 ± 0.64	0.42 ± 0.59	0.0004
Relative gain	0.47 ± 0.20	0.34 ± 17	0.0004
Relative loss	0.28 ± 0.25	0.16 ± 0.21	0.0004
Net gain (mm)	0.63 ± 0.67	0.56 ± 0.60	NS
Loss index	0.59 ± 0.46	0.49 ± 0.96	NS

Data presented are mean value ± 1 SD. Abbreviations as in Table 2.

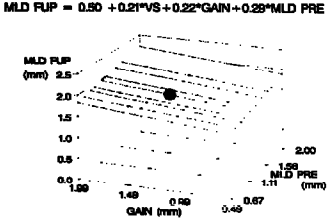

Figure 2. Three-dimensional representation of the linear regression model of minimal lumen diameter (MLD) at follow-up (FUP) after directional atherectomy. Minimal lumen diameter at follow-up is represented on the Y axis, gain at atherectomy on the X axis and minimal lumen diameter before atherectomy (MLD PRE) on the Z axis. The contribution of gain and minimal lumen diameter before atherectomy are represented by assigning the patients to nine equal subgroups (noniles). Lines within the rectangular area represent the median values of these noniles. Positive relations are found between gain and minimal lumen diameter at follow-up and between minimal lumen diameter before atherectomy and minimal lumen diameter at follow-up that do not vary with vessel size. The regression plane shifts progressively upward with increasing vessel size. Dot in the center of the regression plane represents the median value for lumen gain and minimal lumen diameter before atherectomy.

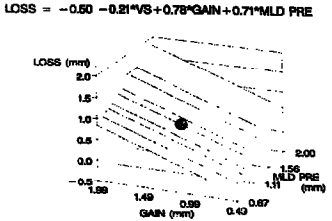

Figure 3. Three-dimensional representation of the linear regression model of lumen loss after directional atherectomy. Loss is represented on the Y axis, gain at atherectomy on the X axis and minimal lumen diameter before atherectomy (MLD PRE) on the Z axis. The contributions of gain and minimal lumen diameter before atherectomy are represented by assigning the patients to nine equal subgroups (noniles). Lines within the rectangular area represent the median values of these noniles. Positive relations are found between gain and loss and between minimal lumen diameter before atherectomy and loss that do not vary with vessel size. The regression plane shifts progressively downward with increasing vessel size. Dot in the center of the regression plane represents the median value for lumen gain and minimal lumen diameter before atherectomy.

dimension, which will shift the regression plane downward (late loss) or upward (late lumen) by 0.21 mm for every increase in vessel size by 1 mm. Both regression equations are as follows: Minimal lumen diameter at follow-up = 0.50 + 0.21 Vessel size + 0.22 Gain + 0.29 Preprocedural minimal lumen diameter; and Absolute loss = −0.50 − 0.21 Vessel size + 0.78 Gain + 0.71 Preprocedural minimal lumen diameter. Therefore, an optimal atherectomy (large late absolute lumen) is thus associated with large vessels, a large gain and a large initial lumen.

Discussion

Restenosis has been shown in animal models (20–22) to be the net result of injury inflicted on the vessel wall during an intervention and the subsequent biologic healing response. High pressure balloon inflation at angioplasty may yield excessive vessel wall damage with disruption of the internal elastic lamina and provoke an intense fibroproliferative reaction. Low pressure balloon inflation and selective plaque removal by directional atherectomy potentially induces less vessel wall trauma. However, it is unknown whether atherectomy is less prone to induce an exuberant healing response after plaque *excision* than balloon *dilation* for an equivalent degree of lumen enlargement measured on angiography. To explore the influence of a device effect on the renarrowing process, we studied matched patients with similar baseline vessel and lesional characteristics and immediate gain after atherectomy or angioplasty.

The major findings of this study are threefold: 1) in matched patients who had the same amount of lumen gain, atherectomy induces more subsequent lumen loss than angioplasty; 2) device type is retained in the multivariate model as a predictor of lumen renarrowing; and 3) the benefit may not be sustained in the long term if atherectomy is not performed optimally.

Matching. Matching study patients with reference patients with similar characteristics can compensate for some of the limitations of nonrandomized studies (23). Furthermore, it may serve as a surrogate for randomized trials (24). Indeed, its analytic value in predicting the outcome of true randomized trials comparing angioplasty with atherectomy (7,10,11) and angioplasty with stenting (24,25) has been demonstrated. In the present study, patients were matched not only for vessel size and lesion severity but also for immediate lumen gain. Therefore, although the patients were treated with two different devices, they have apparently undergone the same extent, albeit by a partially different mechanism, of "vessel wall injury" inflicted by either the balloon or the atherotome. In this matching study, we found that device is an independent predictor of lumen loss (i.e., renarrowing process) and residual lumen at follow-up (i.e., angiographic outcome), which indicates that not only the extent of lumen gain but also the specific mechanism of action (debulking vs. dilating) has an influence on restenosis. In nonmatched observational studies, Kuntz et al. (2,3,6) precluded, by virtue of their study design, the detection of an independent device effect because of the highly statistical differences between their device groups in immediate lumen gain, which is known to be the strongest predictor for late outcome (3,9,10). Although prospective randomized trials are traditionally regarded as the methodology of choice

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for comparing long-term outcome of different interventional procedures, such as the Coronary Angioplasty Versus Excisional Atherectomy Trial (CAVEAT), Canadian Coronary Atherectomy Trial (CCAT), Belgium-Netherlands Stent Trial (BENESTENT) and Stent Restenosis Study (STRESS) (10, 11,25,26), only an approach that includes matching for lumen gain will elucidate a specific device mechanistic effect on lumen renarrowing.

Multivariate analysis. A comprehensive analysis of the restenosis phenomenon has recently demonstrated that the predictors of the residual lumen at follow-up and late lumen loss should be determined simultaneously to assess the restenosis phenomenon from a clinical outcome and biologic process viewpoint (9,27,28). The rationale for inclusion of device, vessel size, preintervention minimal lumen diameter and lumen gain for our multivariate analytic model was 1) to consider the potentially "confounding effect" of one variable on another and 2) to use only absolute and not derived variables that accurately describe the lesion and can be modified by the clinician. Analysis of the late lumen changes of matched patients indicated that device was an independent predictor of the renarrowing process and angiographic outcome. The cutting mechanism of the atherectomy device leads to more lumen loss with a smaller late lumen at follow-up than from balloon angioplasty in patients who had similar postprocedural results. In the near future, this finding that the mechanism as well as extent of lumen improvement determines the subsequent renarrowing process should be analyzed prospectively and confirmed by multicenter studies.

The present results of our matched series may provide further insights into the atherectomy results of the CAVEAT and CCAT trials (10,11). In these randomized trials, as in our matched atherectomy-treated group, the moderate atherectomy procedural gain yielded a postatherectomy minimal lumen of 2.31 mm (our matched atherectomy-treated patients), 2.02 mm (CAVEAT) and 2.34 mm (CCAT). The greater lumen loss during follow-up ultimately led to late residual lumen diameters that were similar to those in the angioplasty-treated group.

Optimal versus suboptimal atherectomy. The present matching study identified a worse long-term outcome of atherectomy when the immediate results are comparable with angioplasty. This indicates that a moderate lumen gain achieved at atherectomy cannot compensate for an increased late lumen loss. That is, if atherectomy is not optimally performed (large immediate gain), the benefit may not be sustained in the long term, and the clinician should thus strive for a large lumen gain at directional atherectomy. To test this hypothesis, we further analyzed our total atherectomy-treated cohort and divided the angiographic results into two equal groups according to the distribution of the postatherectomy lumen diameter. Indeed, the patients who underwent an optimal atherectomy (postatherectomy minimal lumen diameter 2.78 ± 0.27 mm and residual diameter stenosis of 20 ± 8%) had a significantly greater late lumen at follow-up (1.92 ± 0.62 vs. 1.67 ± 0.56 mm, $p = 0.03$) and a conventional restenosis rate of 25% versus 34%. In addition, we also observed a difference in the slope of the gain/loss regression line between the optimal and suboptimal groups (0.35 vs. 0.45), although this difference did not reach statistical significance. This trend toward less proportional loss with larger gains was also found in a preliminary analysis of the CAVEAT data, which suggested a curvilinear relation between immediate gain and late loss with a steeper slope for smaller gains and a shallower slope for larger gains (29). Thus far, the influence of optimal atherectomy on late angiographic outcome is not entirely resolved, and further information will be provided by the imminent BOAT, OARS and EUROCARE trials. Although these will evaluate the effect of optimal atherectomy, BOAT and OARS are designed from the perspective "bigger is better" with emphasis on optimal performance, whereas EUROCARE is designed from the perspective "the more you gain, the more you lose" and combines a large immediate gain with a pharmacologic agent to reduce late lumen loss. In other words, BOAT will increase the "doughnut's hole," whereas EUROCARE will also try to reduce the "doughnut" (9,21,27,28). Ultimately, the restenosis process may be controlled by the combination of a large lumen gain, which will provide a large lumen at follow-up and pharmacologic/biologic/gene therapy to reduce the greater lumen loss.

Clinical implications. The extent of lumen renarrowing is the consequence not only of the extent of lumen improvement but also of the mechanism of vessel wall injury (debulking vs. dilating). Optimal atherectomy seems to be related not only to a large postprocedural lumen or large immediate gain (procedural outcome), but also to large vessel sizes (patient selection). While performing atherectomy, the operator should strive for an optimal procedural result to accommodate an increased intimal hyperplastic response.

Study limitations. We acknowledge that case matching may have led to a selection bias, such as the selection of larger vessels and the representation of left anterior descending coronary artery stenoses. Therefore, we have to acknowledge that the results of this study apply only to such an atherectomy-treated cohort. However, our data indicate that the matched angioplasty lesions are a representative cohort of the angioplasty-treated patients with identical lesion severity as judged by percent diameter stenosis. Furthermore, the matched angioplasty-treated patients had lesion characteristics and outcome similar to the balloon angioplasty-treated patients in the CAVEAT and CCAT trials (10,11). Despite these angiographic similarities between the groups, a difference exists in lesion distribution that was similarly found by others (2,3,6). This is a consequence of dissimilar vessel sizes with smaller left anterior descending coronary arteries than non–left anterior descending coronary vessels. Whether the left anterior descending coronary artery is more prone to restenosis independent of vessel size has yet to be determined (5,6,9,30). To our knowledge there is no pathophysiologic evidence to suggest that one coronary artery should display an inherently more aggressive neointimal healing response to injury than others. Available information on the influence of lesion location on angiographic outcome is conflicting and merits further investigation, particularly with intravascular ultrasound imaging. The American Heart Association/American College of Cardiology lesion classification (31) was not used in this matching

study because "it groups an array of lesions with a heterogeneous morphology and dissimilar percutaneous transluminal coronary angioplasty results" (32). Quantitative morphologic assessment using automated edge detection–derived length, symmetry index, curvature and inflow and outflow angle values may overcome this limitation and also allows a continuous rather than categoric analysis (33).

This study did not assess the influence of recoil on the final outcome of the interventions. However, previous studies have indicated that no significant difference in minimal lumen diameter 24 h after angioplasty was observed (34) when appropriate measures were taken to control vasomotor tone (9). However, the present matching study did take the difference in immediate recoil, which has been reported by Kimball et al. (35), into consideration, because matching was also performed for the postprocedural result.

Although matching seems a suitable statistical technique to explore such relation, this study also indicates one of the limitations of matching. To find 80 angioplasty-treated patients with similar preintervention and postintervention stenosis characteristics to be matched with the 80 consecutive atherectomy-treated patients, 3,637 angioplasty lesions were screened. This indicates that it is unlikely that a similar substudy could be performed to the CAVEAT and CCAT study groups.

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